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| EXAMINER | |
|---|---|
| WESSENDORF, TERESA D | |
| **ART UNIT** | **PAPER NUMBER** |
| 1639 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/930,715 | JENDOUBI, MONCEF | |
| | Examiner | Art Unit | |
| | TERESA WESSENDORF | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *14-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## *DETAILED ACTION*

### *Status of Claims*

Claims 14-21 are p ending and under consideration in the instant Office action.

### *Withdrawn Rejections*

In view of the amendments to the claims and applicants' arguments the 35 USC 112, second paragraph rejection is withdrawn.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-21, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

**New matter Rejection**

Claim 14 drawn to "providing a plurality of antibodies each having a labeling element" is not supported in the as filed specification. The as-filed specification does not define or describe what constitutes a "plurality" of antibodies. Likewise, the broad claimed "labeling element" is not supported in the original specification which discloses specific labeling elements. It appears that amended claim 14, in its entirety, is not supported in the as-filed specification as the numerous present amendments are different from the original claims e.g., claim 1. MPEP 714.02 clearly states that when amendments to the claims are made, applicants are to specifically point out the support in the specification. In the absence of such the entire claim 14 constitutes new matter.

***Written Description Rejection***

The claim method of analyzing differential gene expression in human tissue samples is not adequately described in the specification. The claim human tissue samples would encompass a limitless number of genes or an enormous number of tissue samples expressing said genes.

Applicants state at pages 4-5 of the REMARKS of 9/22/08:

> ….large numbers of antibodies are used to interrogate paired samples from human tissue to determine which genes are expressed or not expressed in different conditions. In one example, samples from normal and cancerous tissue are interrogated by 100, of antibodies to identify genes that are differentially expressed in cancer or, alternatively, expressed in normal tissue and not expressed in cancer. This we find is valuable for identifying diagnostic markers or for identifying genes and proteins that are potential therapeutic targets. The normal and diseased (different biological conditions) **from many different human samples, whether tissues or any biological fluids, from many different individuals for expression analysis or diagnostic applications are analyzed.** (Emphasis added).

The specification provides only a concept or general statement as to the workability of the claimed method. There is not a single or particular tissue that has been shown that expresses a gene/gene product using the antibodies. Neither has applicant proffered any evidence by e.g., prior art teachings that any kind or type of human tissue expresses any kind of genes that can be identified by any type of antibody using the broad process steps. Furthermore that is no disclosure in the specification that all or any human tissues express any kinds of genes to be considered a diagnostic marker. As applicants recognized above not all tissues or any type of tissues expresses a gene particularly a gene of interest. The specification does not provide a working example to aid a skilled artisan to the practice of the claimed method of such enormous scope. The general statements or concepts in the

specification therefore do not suffice as an adequate description of the method especially in an uncertain art as gene expression. The written description requirement clearly requires that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111,). In University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 it was held that: ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which

makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-21,as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 14 is unclear as the inconsistent use of terminologies provide for confusion and ambiguity. For example “two protein samples” as opposed to “at least two samples” or ‘"human tissue sample”. The protein samples specifically (and presumably) contain only protein in a sample. The broad two samples contain components other than the proteins. See also, “labeling element” as opposed to “elements” and “gene expression” as opposed to “an expression product of a gene sequence”. While applicants are permitted to be their own lexicographer however, it carries with it the connotation that

they will use terms consistently throughout their patent. Porter v. Farmers Supply Services Inc., 228 USPQ 4.

B. Non-sequitur for "the at least two distinct biological conditions". Please note the amendments in the prior steps cancel this limitation. Also, "an expression product of a gene sequence" with the cancellation of said phrase in the preceding step." Because of the amendments to the claims cancelling some phrase the claim steps/elements are therefore incomplete and seem to lack correspondence with one another. Claim 14.

C. Claim 17 does not further the base claim 14. The base claim 14 does not recite that in the at least two samples, one is a normal or non-diseased sample.

***Double Patenting***

Claims 14-21, as amended, are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 2 of copending Application No. 10/945,543('543 application) or claims 1-9 of copending application 10/945,784('784). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claimed method is similar to the methods of either the '543 or '784 application except the instant method affixes the protein products in an array as opposed to the copending applications with the antibody affixed

to the array. However, it would have been obvious to affix either the protein products (i.e., antigen) or antibody on the array with a reasonable expectation of achieving the same results i.e., identifying of the protein (antigen) present in the diseased state.

***Response to Arguments***

Applicants state that the provisional double-patenting rejection may be addressed by terminal disclaimer if or when such action becomes appropriate.

In response in the absence of a terminal disclaimer the rejection is maintained.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Rejection(s) Claim Rejections - 35 USC § 102***

Claims 14, and 17-20, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Chenchik et al. (US Patent 6,087,102).

Chenchik et al. disclose arrays of polymeric targets associated with the surface of the support and the method of using the array in high throughput gene expression analysis (see e.g. Abstract; col. 2, lines 3-11, and 51-62; col. 11, lines 3-23). The polymeric targets are biopolymeric compounds that

include naturally occurring polymeric compounds or mimetics or analogues of naturally occurring polymeric compounds. The biopolymeric compounds includes peptides, polypeptides and proteins wherein they derived from cells or tissue extracts, which are derived from normal, disease, or condition state such as cancer or exposure to toxic agents (see e.g. col. 3, lines 13-20, and lines 51-64). The polymeric targets are pattern on the support in a variety of configurations wherein each polymeric target is at a discrete location (see e.g. col. 5, lines 35-47). The method of using the array in high throughput gene expression analysis comprises the step of preparing the probe, contacting the probe with the array under conditions sufficient for probe to bind with corresponding target, removal of unbound probe from the array, and detecting the bound probe (see e.g. col. 8, line 55 thru col. 10, line 45). The probes include peptidic probes such as polyclonal antibodies and a labeled with a detectable label (see e.g. col. 9, lines 18-65). The assay determines both the expression level and the size of the target bound by the probe (see e.g. col. 11, lines 3-23). Thus, the method of Chenchik et al. anticipates the presently claimed invention.

***Response to Arguments***

Applicants argue that the specification of Chenchik provides an array of immobilized proteins arranged according to size which could be probed by several antibodies provided they differ in the binding even to one distinguished by the use of different labels as in an ordinary DNA array. Therefore, the same protein array could only be probed by a small number of antibodies, because only a little number of signal elements, Chenchik's different colored fluorophores, is available. In contrast, in the claimed invention, a matrix of complex biological samples is spotted or associated to a solid support in a physical compartment, and this matrix is repeated several times in as many compartments as there are on the support, and each compartment is interrogated by one antibody from the population of 100 antibodies so that a plurality of proteins in the sample is interrogated by the antibodies simultaneously. Neither the high through-put format nor the use of the number of antibodies corresponding to the number of expressed gene products is anticipated by Chenchik.

In reply, applicants' arguments as to the use of 100 antibodies are not commensurate in scope with at least claim 14, which simply recites a plurality of antibodies. Chenchik

discloses a plurality of antibodies as acknowledged by applicants above of “a small number of antibodies.”

Applicants argue that Chenchik does not contemplate the concept of repetitive compartmentalization of a matrix of proteins that can be interrogated by a number of antibodies simultaneously. However recognize that the Chenchik reference is a conventional example of a protein chip when the size of the member bound to the array assists in the identification of binding events. Applicants acknowledge that the so-called "probe" in the Chenchik disclosure is analogous to the binding antibodies of the present invention. But argue that Chenchik does not correlate specific antibodies used in the reaction to specific genes that may be subject to differential expression analysis. Thus, although Chenchick notes that the array described therein can be used for differential expression analysis, the differential expression does not extend to use at a population of antibodies where each is linked to a particular gene expression product and a particular gene.

In reply, much of applicants’ arguments e.g., the matrix of proteins interrogated by a number of antibodies is not commensurate in scope with the claims. Furthermore, the claims do not recite for any “specific antibodies” rather only a plurality of antibodies. As applicants acknowledged above,

Chenchik discloses the array used for differential expression analysis. Chenchik et al disclose that the binding reaction of a particular antibody is linked to a particular gene for the label, which associated with the probe (antibody), provide a signal only when the probe is specifically bound to the target molecule (gene)(col. 9, lines 58-61; col. 11, lines 12-23), which reads on the claim identifying step.

Claims 14-21, as amended, are rejected under 35 U.S.C. 102(e) as being anticipated by Bandaru (US Patent 6,462,187 B1; filing date of 6/15/2000) for reasons repeated below.

Bandaru discloses a method of comparing the level of expressed polypeptide before and after treatment of the disorder (e.g. biological conditions) (see e.g. col. 4, lines 9-13). The disorder includes cancerous condition (see e.g. col. 10, lines 21-55). The method of detection comprised of detecting the binding interaction of the antibody specific to the expressed polypeptide (see e.g. col. 37, lines 36-47). The method comprise of a two dimensional array having a plurality of addresses each address of the plurality is positionally distinguishable from each other address of the plurality (see e.g. col. 4, lines 35-45; col. 51, lines 37-67). Each address of the plurality can have a unique capture probe such as polypeptide, e.g. an antibody specific for the polypeptide. The plurality of

addresses includes at least 10, 100, 500, 1,000, 5,000, 10,000, 50,000 addresses (see e.g. col. 49, lines 14-16). The array can be use to assay gene expression in a tissue to ascertain tissue specificity of genes in the array (see e.g. col. 49, lines 62-64) or to monitor expression of one or more genes in an array with respect to time for ascertaining differential expression patterns of one or more genes in normal or abnormal cells (see e.g. col. 50, lines 32-45). Additionally, the method of Bandaru discloses the step of containing human protein samples in an array (see e.g. col. 4, lines 9-13) and refer to the analysis of gene expression information in a tissue sample is derived from the differential binding reactions at two discrete sites of the array (see e.g. col. 4, lines 35-40, and 43-45; col. 49, lines 62-64). The method of Bandaru also discloses detecting the signal generated from a labeled attached to the antibody that binds to the probe of the array (see e.g. col. 51, lines 8-67). Therefore the method of Bandaru anticipated the presently claimed method.

***Response to Arguments***

Applicants acknowledge that the method of Bandaru relies on capture probes binding the sites on an array. But argue that the method of Bandaru do not use antibody binding events from an entire population of antibodies across an array for de novo

expression profiling. Bandaru's only disclosure uses a novel thioredoxin to evaluate the presence in a sample (tissue, biopsy, or fluid sample) from a subject before and after treatment, i.e. in two different conditions, and compares the level of this novel thioredoxin polypeptide in these two conditions (see e.g. col. 4, lines 9-13, and col. 10, fines 21-55). Bandaru also describes a possible use of his novel protein, gene, and corresponding antibody in the context of arrays (col. 49, col. 51). Bandaru does not disclose the use of antibodies across the array, the plurality of complex biological samples (i.e. before and after treatment), or the use of a large number of antibodies in a repetitive fashion with a matrix.

In reply, applicants' arguments to the instant use of an entire population of antibodies across an array are unclear as the claims do not recite an entire antibodies but a plurality of antibodies. Therefore the specific components of protein thioredoxin use by Bandaru and the corresponding antibody fully meet the claimed method using broad components therein. Furthermore, Bandaru discloses that the binding reaction of a particular antibody is linked to a particular gene for the label, which associated with the probe (antibody); provide a signal only when the probe is specifically bound to the target

molecule (gene) (col. 50, lines 1-7; col. 51, lines 32-36 and 60-63).

Claims 14-21, as amended, are rejected under 35 U.S.C. 102(e) as being anticipated by Wagner et al. (US Patent 6,329,209 B1; filing date 7/14/1999) for reasons restated below.

Wagner et al. disclosed a method of comparing the protein expression of two cells or a population of cells that have been exposed to different conditions (see e.g. col. 37, lines 19-67). The method comprises an array of protein-capture agents arranged in discrete, known regions of patches (see e.g. col. 9, lines 66-67 to col. 10, lines 1-12). The array can have any number of a plurality of different protein-capture agents (see e.g. col. 11, lines 1-11). For instance, an array comprise of about 10,000 patches would comprise of about 10,000 different protein-capture agents (see e.g. col. 11, lines 28-33). Therefore, the number of different protein-capture agents on an array will vary depending on the application desired (see e.g. col. 11, lines 12-13). The protein-capture agent would include biomolecule such as protein or polynucleotide (see e.g. col. 4, lines 48-67) and would binds specifically to the antibody of interest (see e.g. col. 12, lines 48-52). Additionally, the method of Wagner et al. does perform the method step of containing two tissue samples onto an array to obtain gene expression analysis because Wagner et al.

define an array as an arrangement of entities in a pattern on a substrate (see e.g. col. 6, lines 61-64) and the array have plurality of different protein-capture agents (see e.g. col. 11, lines 1-4) (i.e. pluralities of different protein-capture agents are arranged in a pattern on a substrate). Wagner et al. discloses that protein-capture agents are proteins in a cell that specifically binds to another protein such as an antibody (see e.g. col. 12, lines 50-52). The method of Wagner et al. also disclose detecting the signal generated from a labeled attached to the antibody that binds to the protein-capture agents of the array (see e.g. col. 34, lines 10-43). Therefore the method of Wagner et al. anticipates the presently claimed method.

***Response to Arguments***

Applicants assert that Wagner cannot analyze two protein-containing samples on the SAME antibody array at all. Wagner can only perform that method step on two separate antibody arrays containing the same antibodies, yet contacted or probed with two different samples. This has to be performed in parallel not simultaneously. This is confirmed by the definition of "plurality" of protein binding partners (col. 11 line 57 col. 12 line 9): Wagner talks about a plurality of proteins or gene

expression products yet from a single organism, or single tissue, or single organ.

In response, there is nothing in the claims that state that the human tissue samples are from different organism or tissues.

Applicants argue that Wagner et al. can not perform the method step of containing two tissue samples onto an array to obtain gene expression analysis, but instead rely on two samples using two identical arrays. Wagner et al. cannot perform the step wherein each member of the plurality of antibodies is identified as having specific binding affinity to an expression product of a gene sequence .... "Because this element is necessarily lacking from Wagner et al., Wagner et al. cannot anticipate under Section 102(a).

In reply, Wagner et al. do disclose the instant claimed containing step at e.g. col. 34, lines 10-43; col. 36, lines 51-65; col. 37, lines 54-6) and the method step of claim 15 (col. 26, line 37 thru col. 28, line 26). That is Wagner et al. do disclose that the binding reaction of a particular antibody is linked to a particular gene for the label, which associated with the probe (antibody), provide a signal only when the probe is specifically bound to the target molecule (gene)(see e.g. col. 36, lines 51-65; col. 37, lines 1-36).

Applicants assert that none of the above references meet the limitations of dependent claim 15 wherein antibodies are raised by in vivo immunization of a gene sequence. Applicants are specifically arguing the separate patentability of claim 15 and the remainder of the descendant claims.

In response, applicants' arguments are not commensurate in scope with e.g., claim 15 which do not recite "antibodies are raised by **in vivo immunization of a gene sequence**."

No claim is allowed.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the

organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/

Primary Examiner, Art Unit 1639